

### REMARKS

Claims 12-22 are pending. Claims 20-22 are amended to include a missing definition of  $R^3$  and  $R^4$ . This amendment finds support, for example, at page 8, lines 21-25 of application Serial No. 08/319,411, the contents of which are incorporated into the present patent application (*see*, page 3, line 33 - page 4, line 6). The specification is also amended accordingly.

Claims 12-22 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Although Applicants do not necessarily agree with the rejection, claim 22 is amended to advance prosecution. The claim now reads, in part, "at least one of  $L^1$ - $L^n$  being a naturally occurring nucleobase or non-naturally occurring nucleobase substituted with at least one sterically bulky substituent." Applicants note that on page 9, lines 1-12 of the application, the instantly claimed compositions having at least one "L" group that is a naturally- or non-naturally occurring nucleobase substituted with a sterically bulky group is disclosed. Applicants note that the Advisory Action states that the foregoing amendment would overcome this rejection. As such, withdrawal of the rejection is respectfully requested.

Claims 20 and 21 were rejected under 37 C.F.R. § 1.75(c) as allegedly failing to further limit the claim from which they depend. Claims 20 and 21 are amended to read in independent form.

Finally, the Office Action provisionally rejects claims 12-22 as allegedly obvious under the doctrine of obviousness-type double patenting in view of claims 12-19, 23, 24, and 26 of copending application No. 08/612,661. Without commenting on the appropriateness of the rejection, Applicant submits herewith a terminal disclaimer, thereby overcoming the rejection.

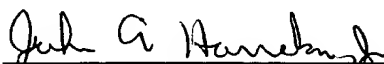
**DOCKET NO.: ISIS-2447**  
**Application No.: 09/142,326**  
**Office Action Dated: December 16, 2003**

**PATENT**

Applicants believe the foregoing constitutes a complete response to the Office Action and submit that all pending claims are in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,

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